PART 13

SELECTED NEUROLOGIC DISORDERS

CHAPTER 66

Tremor and Parkinson Disease

KEY TEACHING POINTS

- The diagnosis of Parkinson disease is based on bedside findings.
- The three cardinal findings of Parkinson disease are bradykinesia, resting tremor, and rigidity. *Parkinsonism* is defined as bradykinesia in combination with either rest tremor, rigidity, or both.
- Some patients with parkinsonism have Parkinson disease. Others have mimicking neurodegenerative disorders collectively called Parkinson-plus or atypical parkinsonian disorders.
- In patients with parkinsonism, the following findings *increase* probability of Parkinson disease: asymmetric onset, absence of atypical features, positive response to levodopa, and asymmetric arm swing when walking.
- In patients with parkinsonism, the following findings *decrease* probability of Parkinson disease: inability to perform a 10-step tandem walk, positive applause sign, and presence of atypical features (i.e., marked autonomic dysfunction, early dementia, pyramidal tract or cerebellar findings, difficulty looking down, use of neuroleptic medications).

I. INTRODUCTION

In a remarkably concise essay written almost 200 years ago, the British physician James Parkinson described in nine pages most of the features we now associate with Parkinson disease—insidious onset, asymmetric resting tremor, bradykinesia, postural instability, sialorrhea, flexed posture, shuffling steps, and festinating gait.[1] One sign Parkinson failed to describe was rigidity, an oversight leading many historians to suggest that Parkinson actually never touched a patient and instead based his conclusions solely on observation.[2] In 1877 Charcot provided the first full account of Parkinson disease that included rigidity.[2]

II. THE FINDING

The three cardinal findings in Parkinson disease are resting tremor, bradykinesia, and cogwheel rigidity (rigidity is discussed fully in Chapter 61). A patient with bradykinesia in combination with either rest tremor, rigidity, or both is said to have **parkinsonism**.[3]

A. TREMOR

A **tremor** is a rhythmic involuntary oscillation of a body part. There are two basic tremors: (1) resting tremor and (2) action tremor.[4-6]

Resting tremors occur when muscles are inactive and the body part is completely supported against gravity. Action tremors occur during voluntary contraction of muscle and are further subdivided into **postural tremors** (e.g., when holding the arms outstretched), **intention tremors** (e.g., when a limb approaches a visually guided target, such as finger-nose-finger testing), **task-related tremors** (e.g., when pouring water from cup to cup), and **isometric tremors** (e.g., when making a fist or gripping the examiner's fingers).* One confusing tremor is a postural tremor (i.e., action tremor) that continues after the examiner supports the outstretched arms (thus mimicking a resting tremor): if such patients are given a glass of water to drink, the amplitude of true postural tremor increases or remains the same as the glass approaches the patient's mouth, whereas that of the genuine resting tremor diminishes in amplitude.

Movement disorder specialists have identified at least a dozen types of tremor, the most common being essential tremor and parkinsonian resting tremor.[4-6] **Essential tremor** is a 4- to 12-Hz† bilateral postural tremor that usually involves the hands or forearms. It may be asymmetric and have an associated kinetic component (i.e., associated intention or task-related component). In contrast, the **parkinsonian resting tremor** (which is only one of the different tremors that may appear in Parkinson disease) is a 4- to 6-Hz "pill-rolling" tremor of the fingertips, hand, or forearm. It begins *asymmetrically,* initially in one hand, followed years later by involvement of the contralateral hand. Essential tremor may involve the jaw, tongue, or head (producing a characteristic rhythmic "nodding yes" or "shaking no" motion); the parkinsonian tremor may involve jaw, lips, or tongue but spares the head.

B. BRADYKINESIA

Patients with bradykinesia have a reduced blink rate. Normal persons blink about 24 ± 15 times per minute, whereas patients with Parkinson disease blink more slowly, approximately 12 ± 10 times per minute. Severely symptomatic patients blink only 5 to 6 times per minute.[7,8] The contrast between the reduced spontaneous blink rate but exaggerated reflex blink rate (during glabellar reflex testing, see Chapter 63) is striking in Parkinson disease. During treatment with levodopa, the spontaneous blink rate increases as the reflex rate during glabellar testing diminishes.[9,10]

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* *Intention tremor* and *task-related tremor* are sometimes collectively called *kinetic tremors* (i.e., action tremors appearing during movement).

† "Hz" indicates "hertz", a unit of frequency equal to one cycle per second. A parkinsonian tremor of 5 Hz, therefore, has 300 oscillations per minute (i.e., 5 × 60), thus explaining why this tremor sometimes produces electrocardiographic artifacts mimicking tachyarrhythmias (e.g., atrial flutter or ventricular tachycardia).

C. ATYPICAL FEATURES OF PARKINSON DISEASE

Confirming the diagnosis of Parkinson disease during life is difficult because the disorder still lacks biochemical, genetic, or imaging diagnostic standards. In patients diagnosed during life with Parkinson disease, 10% to 25% have an alternative diagnosis discovered at postmortem examination.[11-15] These alternative mimicking conditions consist of a variety of neurodegenerative disorders collectively referred to as **Parkinson-plus syndromes** (or atypical parkinsonian syndromes), disorders that tend to progress more rapidly, present more symmetrically, and respond less well to levodopa than does Parkinson disease.[16] Several clinical clues, called **atypical features**, suggest one of these mimicking Parkinson-plus disorders: (1) marked autonomic dysfunction (e.g., postural hypotension, neurogenic bladder or bowel), (2) early severe dementia, (3) pyramidal tract findings (i.e., hyperreflexia, spasticity, or Babinski sign; see Chapter 61), (4) cerebellar findings (i.e., limb ataxia, gait ataxia, or nystagmus; see Chapter 65), (5) supranuclear gaze palsy (i.e., difficulty looking down), (6) use of neuroleptic medications, (7) multiple prior strokes, and (7) encephalitis at the time of onset of symptoms.[3,11]

The most common Parkinson-plus syndromes are multiple system atrophy, progressive supranuclear palsy, and vascular parkinsonism.‡

D. TANDEM GAIT TESTING

The gait of patients with Parkinson disease has a much narrower base than that of most Parkinson-plus patients, leading neurologists to wonder whether tandem gait testing (see also Chapter 7) might more easily provoke imbalance in patients with Parkinson-plus disorders, thus distinguishing them from Parkinson disease. According to this hypothesis, inability to complete 10 tandem steps would suggest a Parkinson-plus disorder, not Parkinson disease.

E. APPLAUSE SIGN (CLAPPING TEST)

The **applause sign** refers to the tendency of some patients to continue clapping their hands in response to instructions to clap three times. Initially the sign was proposed as a way to distinguish progressive supranuclear palsy (more than three claps, or a positive applause sign) from Parkinson disease (only three claps),[17] although subsequently a positive applause sign has been noticed in many other neurodegenerative disorders, especially those causing frontal lobe dysfunction.[18] To perform the sign, the clinician asks the patient to clap three times as quickly as possible and then demonstrates the clapping. The patient's response is normal if he or she claps just three times and abnormal if there are more than three claps. The exact cause of the abnormal applause sign is unknown, although many believe it could be related to frontal disinhibition.[19,20]

III. CLINICAL SIGNIFICANCE: DIAGNOSING PARKINSON DISEASE

In patients with combinations of tremor, bradykinesia, and rigidity (i.e., patients with parkinsonism), the following symptoms increase probability of Parkinson

‡**Multiple system atrophy** has three phenotypes: *Shy-Drager syndrome* (early autonomic insufficiency is prominent), *olivopontocerebellar atrophy* (cerebellar signs are prominent), and *striatonigral degeneration* (both cerebellar and pyramidal tract signs are prominent). **Vascular parkinsonism** refers to parkinsonism that appears abruptly after a stroke; neuroimaging reveals subcortical or deep brain infarction.

disease: the complaint of feet suddenly freezing in doorways (likelihood ratio [LR] = 4.4), voice progressively becoming softer (LR = 3.2), or handwriting becoming progressively smaller (i.e., micrographia, LR = 2.7).[21,22]

The following physical findings also increase probability of pathologic Parkinson disease: the combined presence of all three cardinal features, asymmetric onset, and no atypical features (LR = 4.1; EBM Box 66.1), a good response to levodopa (LR = 4.1), and asymmetric arm swing when walking (LR = 2.7). Inability to perform 10 tandem steps (LR = 0.2) and positive applause sign (LR = 0.3) decrease probability of Parkinson disease. Another sign similar to the 10 tandem step test is the **bicycle sign:** in patients with parkinsonism (who were bicycle riders just before the onset of their symptoms), the inability to continue riding their bicycle decreases probability of Parkinson disease (positive bicycle sign, LR = 0.1) and thus increases probability of a Parkinson-plus disorder.[38]

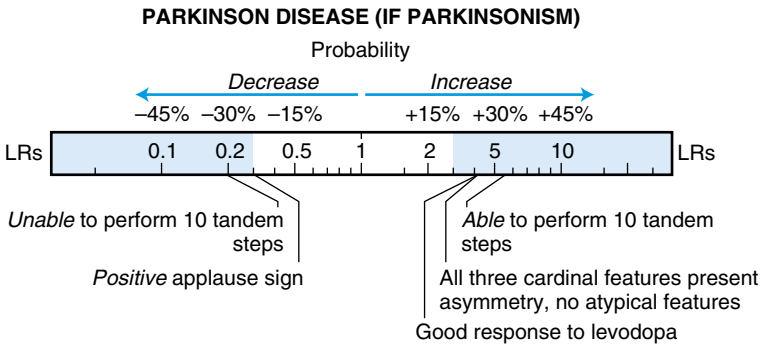
EBM BOX 66.1
*Suspected Parkinson Disease**

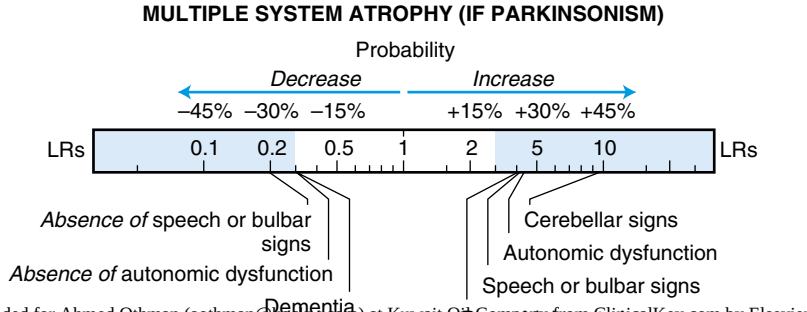
Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Diagnosing Parkinson Disease				
Unable to perform 10 tandem steps [23,24]	8-33	9-18	**0.2**	**5.4**
Asymmetric arm swing[25]	59	79	**2.7**	0.5
Positive applause sign[17-19,26]	3-30	27-42	**0.3**	2.4
Tremor, Bradykinesia, Rigidity[11]				
3 of 3 present	64	71	2.2	0.5
3 of 3 present, asymmetry, no atypical features	68	83	**4.1**	0.4
Good response to levodopa[27,28]	86-98	53-90	**4.1**	**0.2**
Diagnosing Multiple System Atrophy				
Rapid progression[29,30]	54-64	78	2.5	0.6
Absence of tremor[29-31]	39-91	39-76	NS	NS
Speech and/or bulbar signs[29]	87	79	**4.1**	**0.2**
Autonomic dysfunction[29-31]	73-84	74-90	**4.3**	**0.3**
Cerebellar signs[29,31]	32-44	90-99	**9.5**	0.7
Pyramidal signs[29,31]	31-50	85-93	**4.0**	NS
Dementia[29,31]	17-25	36-45	**0.3**	1.9
Diagnosing Progressive Supranuclear Palsy				
Downgaze palsy AND postural instability within first year of symptoms[32,33]	39-50	97-99	**18.0**	0.6

EBM BOX 66.1
Suspected Parkinson Disease—cont'd*

Finding (Reference)†	Sensitivity (%)	Specificity (%)	Likelihood Ratio‡ if Finding Is	
			Present	Absent
Diagnosing Vascular Parkinsonism				
Pyramidal tract signs[34-37]	26-68	95-99	**21.3**	0.5
Lower body parkinsonism[34-36]	59-69	88-91	**6.1**	0.4

*Diagnostic standard: For *Parkinson disease*, careful clinical observation[17-19,23-26] or postmortem examination of brain revealing depletion of nigral pigmented neurons with Lewy bodies in remaining nerve cells (all other studies); for *progressive supranuclear palsy,* pathologic examination; for *vascular parkinsonism,* infarction on neuroimaging or postmortem examination revealing cerebrovascular disease and absence of depigmentation and Lewy bodies.[37]
†Definition of findings: For *atypical features*, see text; for *rapid progression,* the appearance of unsteadiness and tendency to fall at initial visit[29] or within 3 years of onset of first symptom;[30] for *speech or bulbar findings,* dysarthria, dysphagia, and excessive sialorrhoea; for *autonomic dysfunction,* symptomatic postural hypotension, urinary urge or fecal incontinence, or neurogenic bladder[29] or abnormalities on formal testing of cardiovascular reflexes;[30] for *cerebellar findings, applause sign,* and *pyramidal tract findings*, see text.
All LRs apply *only* to patients with suspected Parkinson disease (i.e., combinations of tremor, bradykinesia, and rigidity).
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, Not Significant.
Click here to access calculator





In patients with parkinsonism the presence of cerebellar signs (LR = 9.5; see EBM Box 66.1), autonomic dysfunction (LR = 4.3), or speech/bulbar signs (LR = 4.1) increases the probability of multiple system atrophy. The combination of a downgaze palsy and early postural instability from axial rigidity increases probability of progressive supranuclear palsy (LR = 18). The presence of pyramidal tract signs increases probability of vascular parkinsonism (LR = 21.3) and multiple system atrophy (LR = 4). Parkinsonian findings confined to the legs suggest vascular parkinsonism (LR = 6.1), as does abrupt onset of parkinsonian findings (LR = 21.9).[35,36]

The references for this chapter can be found on www.expertconsult.com.

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